Claims

1. An isolated nucleic acid molecule, comprising

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and SEQ ID NO:22 and which codes for a PAX8-PPARγ1 polypeptide,

(b) deletions, additions and substitutions of (a), which code for a respective PAX8-PPARγ1 polypeptide,

(c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and

(d) complements of (a), (b) or (c).

2. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and SEQ ID NO:22.

3. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule codes for a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:23.

4. An isolated nucleic acid molecule selected from the group consisting of

(a) a unique fragment of a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and SEQ ID NO:22 and

(b) complements of (a)

provided that the unique fragment includes a sequence of contiguous nucleotides which is not identical to any sequence from the sequence group consisting of

(1) sequences having the database accession numbers of Table 1, and

(2) complements of (1).

5. The isolated nucleic acid molecule of claim 4, wherein the sequence of contiguous nucleotides is selected from the group consisting of:

(1) at least two contiguous nucleotides nonidentical to the sequence group,
(2) at least three contiguous nucleotides nonidentical to the sequence group,
(3) at least four contiguous nucleotides nonidentical to the sequence group,
(4) at least six contiguous nucleotides nonidentical to the sequence group,
(5) at least eight contiguous nucleotides nonidentical to the sequence group,
(6) at least ten contiguous nucleotides nonidentical to the sequence group.

6. The isolated nucleic acid molecule of claim 4 or 5, wherein the unique fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20 nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides and 200 nucleotides.

7. The isolated nucleic acid molecule of claim 4 or 5, wherein the unique fragment encodes a peptide which is a fragment of a polypeptide having a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:23.

8. The isolated nucleic acid molecule of claim 6, wherein the unique fragment encodes a peptide which is a fragment of a polypeptide having a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:23.

9. An expression vector comprising the isolated nucleic acid molecule of claims 1, 2 or 3, operably linked to a promoter.

10. An expression vector comprising the isolated nucleic acid molecule of claim 7 operably linked to a promoter.

11. An expression vector comprising the isolated nucleic acid molecule of claim 8, operably linked to a promoter.

12. A host cell transformed or transfected with the expression vector of claim 9.

13. A host cell transformed or transfected with the expression vector of claim 10.

14. A host cell transformed or transfected with the expression vector of claim 11.

15. An isolated polypeptide encoded by the isolated nucleic acid molecule of claim 1, wherein the polypeptide is a PAX8-PPARγ1 polypeptide.

16. The isolated polypeptide of claim 15, wherein the isolated polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:23.

17. An isolated peptide comprising a fragment of the isolated polypeptide of claim 16, of sufficient length to represent a sequence unique within the human genome and to identify a PAX8-PPARγ1 polypeptide.

18. The isolated peptide of claim 17, wherein the fragment is immunogenic.

19. The isolated peptide of claim 17, wherein the peptide comprises at least 6, 8, 9, 10, 11, 12, 14, 16, 18 or 20 contiguous amino acids having a sequence of a fragment of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:23.

20. The isolated peptide of claim 16, wherein the peptide comprises a sequence selected from a group consisting of SEQ ID NO:8, SEQ ID NO:10 and SEQ ID NO:12.

21. An isolated nucleic acid molecule comprising a sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:9 and SEQ ID NO:11.

22. A replicable vector comprising a nucleic acid molecule of claim 21.

23. A host cell comprising a replicable vector including a nucleic acid molecule of claim 21.

24. A composition comprising

an isolated binding agent that binds selectively to a PAX8-PPARγ1 molecule.

25. The composition of claim 24, wherein the PAX8-PPARγ1 molecule is a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:23 or a fragment thereof.

26. The composition of claim 24, wherein the PAX8-PPARγ1 molecule is a nucleic acid molecule comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:22 or a fragment thereof.

27. The composition of claim 24, wherein the isolated agent is a peptide.

28. The composition of claim 27, wherein the peptide is an antibody, or a fragment thereof.

29. The composition of claim 28, wherein the antibody is a humanized antibody or a chimeric antibody.

30. The composition of claim 24, wherein the isolated agent is conjugated to a detectable label.

31. The composition of claim 30, wherein the detectable label is selected from the group consisting of a radioactive label, an enzyme, a biotin molecule, an avidin molecule or a fluorochrome.

32. The composition of claim 24, wherein the isolated agent is a nucleic acid molecule.

33. A method of identifying the presence of PAX8-PPARγ1 molecule in a sample comprising

analyzing the sample for the presence of a PAX8-PPARγ1 nucleic acid molecule or a PAX8-PPARγ1 polypeptide.

34. The method of claim 33, further comprising

contacting the sample with at least two nucleic acid amplification primers, wherein a first nucleic acid amplification primer is capable of hybridizing to a PAX8 nucleic acid molecule and a second nucleic acid amplification primer is capable of hybridizing to a PPARγ nucleic acid molecule,

amplifying a primed nucleic acid molecule which hybridizes to the first and the second nucleic acid amplification primers; and

detecting the presence of an amplified nucleic acid molecule in the sample.

35. The method of claim 33, further comprising

contacting the sample with at least two nucleic acid probes, wherein a first nucleic acid probe is capable of hybridizing to a PAX8 nucleic acid molecule and a second nucleic acid probe is capable of hybridizing to a PPARγ nucleic acid molecule, and

detecting the presence of a nucleic acid molecule in the sample which hybridizes to both the first and the second nucleic acid probes.

36. The method of claim 33, further comprising

contacting the sample with a nucleic acid probe which is capable of hybridizing to a PAX8-PPARγ1 nucleic acid fusion juncture, and

detecting the presence of a nucleic acid molecule in the sample which hybridizes to the nucleic acid probe.

37. The method of claim 36, wherein the PAX8-PPARγ1 nucleic acid fusion juncture comprises a sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:9 and SEQ ID NO:11.

38. The method of claim 33, further comprising

contacting the sample with at least two binding agents, wherein a first binding agent is capable of selectively binding to a PAX8 polypeptide and a second binding agent is capable of selectively binding to a PPARγ polypeptide; and

detecting the presence of a PAX8-PPARγ1 polypeptide in the sample which binds both the first and second binding agents.

39. The method of claim 33, further comprising

contacting the sample with a binding agent which is capable of selectively binding to a PAX8-PPARγ1 polypeptide fusion juncture, and

detecting the presence of a PAX8-PPARγ1 polypeptide in the sample which selectively binds the binding agent.

40. The method of claim 38 or 39, wherein the binding agent is an antibody or a fragment thereof.

41. A method for treating a subject having a disorder characterized by the presence of a PAX8-PPARγ1 nucleic acid molecule comprising

administering a PPARγ ligand to a subject in need of such treatment in an amount effective to treat the subject provided the subject is not otherwise in need of PPARγ ligand treatment.

42. The method of claim 41, wherein the PPARγ ligand is selected from the group consisting of 5-[4-[2-(5-ethylpyridin-2-yl)ethoxyl]benzyl]thiadiazolidine-2,4-dione: (pioglitazone); 5-[4-[(1-methylcyclohexyl)methoxy]benzyl]thiadiazolidine-2,4-dione: (ciglitazone); 5-[(2-benzyl-2,3-dihydrobenzopyran)-5-ylmethyl]thiadiazoline-2,4-dione: (englitazone); 5-[(2-alkoxy-5-pyridyl)methyl]-2,4-thiazolidinedione; 5-[(substituted-3-pyridyl)methyl]-2,4-thiazolidinedione; 5-[4-(2-methyl-2-phenylpropoxy)benzyl]thiazolidine-2,4-dione; 5-[4-[3-(4-methyoxyphenyl)-2-oxooxazolidin-5-yl]-methoxy]benzyl-2,4-thiazolidinedione; 5-[4-[3-(3,4-difluorophenyl)-2-oxooxazolidin-5-yl]-methoxy]benzyl-2,4-thiazolidinedione; 5-[4-[3-(4-chloro-2-fluorophenyl)-2-oxooxazolidin-5-yl]methoxy]benzyl-2,4-thiazolidinedione; 5-[4-[3-(4-trifluoromethoxyphenyl)-2-oxooxazolidin-5-yl]methoxy] benzyl-2,4-thiazolidinedione; 5-[4-[3-(4-trifluoromethylphenyl)-2-oxooxazolidin-5-yl]methoxy]benzyl-2,4-thiazolidinedione; 5-[4-[2-[3-(4-trifluoromethylphenyl)-2-oxooxazolidin-5-yl]ethoxy]benzyl]-2,4-thiazolidinedione; 5-[4-[2-[3-(4-chloro-2-fluorophenyl)-2-oxooxazolidin-5-yl]ethoxy]benzyl]-2,4-thiazolidinedione; 5-[4-[3-(4-

pyridyl)-2-oxooxazolidin-5-yl]methoxy]-benzyl-2,4-thiazolidinedione; 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-2,4-thiazolidinedione: (troglitazone); 4-(2-naphthylmethyl)-1,2,3,5-oxathiadiazole-2-oxide; 5-[4-[2-[N-(benzoxazol-2-yl)-N-methylamino]ethoxy]benzyl]-5-methylthiazolidine-2,4-dione; 5-[4-[2-[2,4-dioxo-5-phenylthiazolidin-3-yl)ethoxy]benzyl]thiazolidine-2,4-dione; 5-[4-[2-[N-methyl-N-(phenoxycarbonyl)amino]ethoxy]benzyl]thiazolidine-2,4-dione; 5-[4-(2-phenoxyethoxy)benzyl]thiazolidine-2,4-dione; 5-[4-[2-(4-chlorophenyl)ethylsulfonyl]benzyl]thiazolidine-2,4-dione; 5-[4-[3-(5-methyl-2-phenyloxazol-4-yl)propionyl]benzyl]thiazolidine-2,4-dione; 5-[[4-(3-hydroxy-1-methylcyclohexyl)methoxy]benzyl]thiadiazolidine-2,4-dione; 5-[4-[2-(5-methyl-2-phenyloxazol-4-yl)ethoxyl]benzyl]thiadizolidione-2,4-dione; 5-[[2-(2-naphthylmethyl)benzoxazol]-5-ylmethyl]thiadiazoline-2,4-dione; 5-[4-[2-(3-phenylureido)ethoxyl]benzyl]thiadiazoline-2,4-dione; 5-[4-[2-[N-(benzoxazol-2-yl)-N-methylamino]ethoxy]benzy]thiadiazoline-2,4-dione; 5-[4-[3-(5-methyl-2-phenyloxazol-4-yl)propionyl]benzyl]thiadiazoline-2,4-dione; 5-[2-(5-methyl-2-phenyloxazol-4-ylmethyl)benzofuran-5-ylmethyl]-oxazolidine-2,4-dione; 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl]thiazolidine-2,4-dione; and 5-[4-[2-[N-(benzoxazol-2-yl)-N-methylamino]ethoxy]benzyl]-oxazolidine-2,4-dione.

43. The method of claim 41, wherein the disorder is cancer.

44. The method of claim 43, wherein the cancer is follicular carcinoma.

45. The method of claim 41, wherein the agent is administered directly to a tissue.

46. The method of claim 45, wherein the tissue is thyroid tissue.

47. A method of locating cells containing a PAX8-PPARγ1 polypeptide comprising contacting a cell with a radiolabeled binding agent which is capable of specifically binding to a PAX8-PPARγ1 polypeptide fusion juncture, and

observing the locus of radioactivity in the cell.

48. The method of 47, wherein the cell is contacted with the radiolabeled binding agent in vivo.

49. A method of delivering a toxic substance to a subject having cells containing a PAX8-PPARγ1 polypeptide comprising

administering to the subject a toxin-conjugated binding agent which is capable of binding to a PAX8-PPARγ1 polypeptide fusion juncture.

50. A method of reducing expression of an PAX8-PPARγ1 nucleic acid molecule in a cell having a PAX8-PPARγ1 nucleic acid molecule comprising:

introducing a PAX8-PPARγ1 antisense nucleic acid molecule into a cell, and

allowing the PAX8-PPARγ1 antisense nucleic acid molecule to hybridize to a sense PAX8-PPARγ1 nucleic acid molecule thereby inhibiting expression of the sense PAX8-PPARγ1 nucleic acid molecule.

51. A method of inhibiting production of a PAX8-PPARγ1 polypeptide comprising

administering to a cell containing a PAX8-PPARγ1 nucleic acid molecule a ribozyme that cleaves a PAX8-PPARγ1 nucleic acid molecule in an amount effective to inhibit production of the PAX8-PPARγ1 polypeptide.

52. A transgenic non-human animal having somatic and germ line cells that contain a PAX8-PPARγ1 nucleic acid molecule of claim 1, wherein expression of the PAX8-PPARγ1 nucleic acid molecule results in the animal having abnormal cell growth.

53. A method of screening for an agent that inhibits the production of a PAX8-PPARγ1 polypeptide, comprising

determining the level of a PAX8-PPARγ1 polypeptide in the absence of a compound,

determining the level of a PAX8-PPARγ1 polypeptide in the presence of the compound, and

comparing the level of a PAX8-PPARγ1 polypeptide in the presence and absence of the compound wherein a decrease in the level of a PAX8-PPARγ1 polypeptide in the presence

of the compound is indicative of an agent that inhibits the production of a PAX8-PPARγ1 polypeptide.

54. The method of claim 53, wherein the agent inhibits transcription of a PAX8-PPARγ1 nucleic acid molecule.

55. The method of claim 53, wherein the agent inhibits translation of a PAX8-PPARγ1 nucleic acid molecule.

56. The method of claim 53, wherein the method is performed in a cell free system.

57. The method of claim 53, wherein the method is performed in a transgenic, non-human animal.

58. A method for treating a subject having a disorder characterized by the presence of a PAX8-PPARγ1 nucleic acid molecule comprising

administering an agent to a subject in need of such treatment in an amount effective to treat the subject

wherein the agent interferes with PAX8-PPARγ1 molecule binding or PAX8-PPARγ1 molecule function, provided the agent is not a PPARγ ligand.

59. The method of claim 58, wherein the agent interferes with gene transcription.

60. The method of claim 58, wherein the agent promotes gene transcription.

61. The method of claim 58, wherein the cancer is carcinoma.

62. The method of claim 61, wherein the carcinoma is thyroid follicular carcinoma.